

AMENDMENTS

Amendments to the Claims:

This listing replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (currently amended) A method for selecting a siRNA for a target gene, wherein said siRNA comprises 19 – 25 nucleotide ~~nucleoside~~ base pairs, said method comprising the steps:
 - (a) selecting a target gene;
 - (b) generating a set of candidate siRNA molecules, wherein each of said candidate siRNA molecules comprises an antisense region of at least 19 bases that ~~is~~ are at least 79% ~~substantially~~ complementary to a region of the target gene;
 - (c) applying a criterion to each of said candidate siRNA molecules, wherein the criterion is selected from the group consisting of: (i) the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region; (ii) the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region; (iii) the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region; (iv) the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region; and (v) the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide; and

(d) selecting a candidate siRNA from the set of candidate siRNA molecules of step (b) as said siRNA for the target gene, if said candidate siRNA satisfies said criterion.

2. (canceled)

3. (canceled)

4. (canceled)

5. (canceled)

6. (currently amended) A method for developing an siRNA algorithm for generating an output selecting siRNA, said method comprising the steps:

(a) selecting a set of siRNA, wherein the set of siRNA comprises a plurality of siRNA that are directed against sequences in a target gene and each siRNA within said plurality of siRNA comprises a sense region of 19 – 30 bases;

(b) determining the ability of each siRNA of said plurality of siRNA to silence the target gene;

(c) correlating ~~the presence or absence of~~ one or more variables with said ability of each siRNA of said plurality of siRNA to silence said target gene, wherein said one or more variables comprises, ~~are selected from the group consisting of total GC content, melting temperature of the siRNA, GC content at positions 15–19, the presence or absence of a particular nucleotide at at least one of positions 1 – 19 of a sense sequence within the sense region, wherein when the sense region is 20 – 30 bases, bases that are not within said sense sequence occupy positions 1 to 11 and positions 1 to 11 of the sense region are located at the 5' end of the sense region a particular position and the number of times that the same nucleotide repeats within a given sequence~~; and

(d) developing an algorithm for selecting siRNA wherein said algorithm comprises said one or more variables, and when the algorithm is applied to a candidate siRNA ~~sequence~~ the algorithm is capable of generating a value that is dependent on the satisfaction of said one or more variables

and said algorithm outputs to a user or computer storage device either
said value or a relative ranking of a plurality of candidate siRNAs to
which said algorithm is applied.

7. (canceled)

8. (canceled)

9. (canceled)

10. (canceled)

11. (canceled)

12. (canceled)

13. (canceled)

14. (canceled)

15. (canceled)

16. (canceled)

17. (canceled)

18. (canceled)

19. (canceled).

20. (canceled)

21. (canceled)

22. (canceled)

23. (canceled)

24. (canceled)

25. (canceled)

26. (canceled)

27. (currently amended) The method according to claim 6, wherein in step (c) said ability of each siRNA of said plurality of siRNA to silence said target gene is further correlated with said algorithm comprises two or more at least one variables selected from the group consisting of: the total GC content, melting temperature of the siRNA, GC content at positions 15 -19, ~~the presence or absence of one or more particular nucleotides at one or more particular positions~~, and the number of times that the same nucleotide repeats contiguously in a stretch of four or more units within a given sequence.

28. (currently amended) The method according to claim 6 27, wherein in step (c) said ability of each siRNA of said plurality of siRNA to silence said target gene is further correlated with said algorithm comprises at least two three or more variables selected from the group consisting of: the total GC content, melting temperature of the siRNA, GC content at positions 15 -19, ~~the presence or absence of one or more particular nucleotides at one or more particular positions~~, and the number of times that the same nucleotide repeats contiguously in a stretch of four or more units within a given sequence.

29. (currently amended) The method according to claim 6 ~~28~~, wherein in step (c) said ability of each siRNA of said plurality of siRNA to silence said target gene is further correlated with said algorithm comprises at least three ~~four or more~~ variables selected from the group consisting of: the total GC content, melting temperature of the siRNA, GC content at positions 15 -19, ~~the presence or absence of one or more particular nucleotides at one or more particular positions~~, and the number of times that the same nucleotide repeats contiguously in a stretch of four or more units within a given sequence.
30. (canceled)
31. (canceled)
32. (canceled)
33. (canceled)
34. (canceled)
35. (canceled)
36. (canceled)
37. (canceled)
38. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region.

39. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region.
40. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region.
41. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region.
42. (previously presented) The method according to claim 1, wherein the criterion is: the first 5' position of the antisense region has either A or U and the last 3' position of the antisense region had neither A nor U.
43. (currently amended) A method for selecting a siRNA for a target gene, wherein said siRNA comprises 19 – ~~30~~ 25 nucleoside nucleotide base pairs, said method comprising the steps:
- (a) selecting a target gene;
 - (b) generating a set of candidate siRNA molecules, wherein each of said candidate siRNA molecules comprises a sense region of 19 – 30 bases, wherein said sense region comprises a sense sequence region of at least 19 bases that is are at least 79% ~~substantially~~ similar to a region of the target gene;
 - (c) applying a set of one or more criteria selected from the group consisting of the presence of A at position 19 of the sense sequence region, the presence of A at position 3 of the sense sequence region, the presence of U at position 10 of the

sense sequence region, the presence of A at position 14 of the sense sequence region, the absence of C at position 19 of the sense sequence region, the absence of G at position 13 of the sense sequence region, the absence of U at position 5 of the sense sequence region and the absence of A at position 11 of the sense sequence region wherein said sense sequence occupies positions 1 – 19 of the sense region, and wherein when said siRNA is 20 – 30 base pairs, bases that are not within said sense sequence occupy positions 1 to 11 and positions 1 to 11 are located at the 5' end of the sense region; and

(d) selecting a candidate siRNA from the set of candidate siRNA molecules of step (b) as said siRNA for the target gene, if said candidate siRNA satisfies said one or more criteria.

44. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of A at position 19 of the sense sequence region.
45. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of A at position 3 of the sense sequence region.
46. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of U at position 10 of the sense sequence region.
47. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of A at position 14 of the sense sequence region.
48. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of C at position 19 of the sense sequence region.
49. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of G at position 13 of the sense sequence region.

50. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of U at position 5 of the sense sequence region.
51. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of A at position 11 of the sense sequence region.
52. (currently amended) The method according to claim 43 further comprising applying one or more additional criteria selected from the group consisting of: a GC content between about 30% and 52%, at least 2 A or U bases at positions 15 – 19 of the sense sequence region, and a internal repeat that is not stable at greater than 50°C, and ~~wherein selecting said candidate siRNA for the target gene if said candidate siRNA~~ satisfies said one or more additional criteria.
53. (previously presented) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies at least two criteria selected from the group consisting of: the presence of A at position 19 of the sense sequence region, the presence of A at position 3 of the sense sequence region, the presence of U at position 10 of the sense sequence region, the presence of A at position 14 of the sense sequence region, the absence of C at position 19 of the sense sequence region, the absence of G at position 13 of the sense sequence region, the absence of U at position 5 of the sense sequence region, and the absence of A at position 11 of the sense sequence region.
54. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies at least three criteria selected from the group consisting of: the presence of A at position 19 of the sense sequence region, the presence of A at position 3 of the sense sequence region, the presence of U at position 10 of the sense sequence region, the presence of A at position 14 of the sense sequence region, the absence of C at position 19 of the sense sequence region, the absence of G at position 13 of the sense

sequence region, the absence of U at position 5 of the sense sequence region, and the absence of A at position 11 of the sense sequence region.

55. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies at least four criteria selected from the group consisting of: the presence of A at position 19 of the sense sequence region, the presence of A at position 3 of the sense sequence region, the presence of U at position 10 of the sense sequence region, the presence of A at position 14 of the sense sequence region, the absence of C at position 19 of the sense sequence region, the absence of G at position 13 of the sense sequence region, the absence of U at position 5 of the sense sequence region, the absence of A at position 11 of the sense sequence region, a GC content between about 30% and 52%, at least 2 A or U bases at positions 15 – 19 of the sense sequence region, and a internal repeat that is not stable at greater than 50°C.
56. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies at least five criteria selected from the group consisting of: the presence of A at position 19 of the sense sequence region, the presence of A at position 3 of the sense sequence region, the presence of U at position 10 of the sense sequence region, the presence of A at position 14 of the sense sequence region, the absence of C at position 19 of the sense sequence region, the absence of G at position 13 of the sense sequence region, the absence of U at position 5 of the sense sequence region, the absence of A at position 11 of the sense sequence region, a GC content between about 30% and 52%, at least 2 A or U bases at positions 15 – 19 of the sense sequence region, and a internal repeat that is not stable at greater than 50°C.
57. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria: a GC content between about 30% and 52%, at least 2 A or U bases at position 15 –19 of the sense sequence region, A at position 19 of the

sense sequence region, A at position 3 of the sense sequence region, a base other than C at position 19 of the sense sequence region, a base other than G at position 13 of the sense sequence region, and an internal repeat that is not stable at a temperature of greater than 50°C.

58. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria: a GC content of between 30% and 52% and a base other than G at position 13 of the sense sequence region.
59. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria: a base other than C at position 19 of the sense sequence region and a base other than G at position 13 of the sense sequence region.
60. (currently amended) The method according to claim 43, wherein said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria: a GC content of between 30% and 52%, a base other than G at position 13 of the sense sequence region and an internal repeat that is not stable at a temperature of greater than 50°C.